Research Digest

Slow-release morphine was not more effective than methadone in reducing neonatal abstinence syndrome

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QUESTION

In pregnant women who are opioid dependent or polysubstance abusers, is slow-release morphine with an intermediate half-life (16 hours) more effective than methadone in reducing the neonatal abstinence syndrome in their newborn infants?

DESIGN

A randomized, unblinded, controlled trial with a mean follow-up of 15 weeks (follow-up information supplied by author).

SETTING

A drug addiction outpatient clinic at a university hospital in Vienna, Austria.

PARTICIPANTS

A total of 48 pregnant women (mean age, 26 years; mean gestation, 22 weeks) who were dependent on opioids or abused polysubstances (mean duration, 61 months) were willing to follow the maintenance program and to avoid using illegal drugs. Follow-up was complete.

INTERVENTION

Women were allocated to receive oral slow-release morphine tablets twice a day (n=24) or an oral methadone solution once a day (n=24). A flexible-dose regimen was used, and the mean dose at delivery was 53 mg for methadone and 300 mg for slow-release morphine. All women received psychosocial counseling twice a week and group psychotherapy once a week.

MAIN OUTCOME MEASURES

Neonatal abstinence syndrome was assessed every 6 hours using the Finnegan score. Other outcomes were illegal drug consumption (assessed by urinalysis and new injection sites), nicotine dependence (Fagerström questionnaire), and fetal distress.

MAIN RESULTS AND CONCLUSIONS

Neonatal infants born to mothers in the group receiving methadone and the group receiving slow-release morphine did not differ in the duration of the neonatal abstinence syndrome (16 days in the methadone group vs 21 days in the slow-release morphine group; P=0.18). The women's mean daily dose of slow-release morphine or methadone was not associated with the duration of neonatal abstinence syndrome (r=0.53, and P=0.20 for methadone; r=0.39, and P=0.34 for slow-release morphine). More women in the methadone group than in the slow-release morphine group used additional opiates (P<0.05) (table) and benzodiazepines (P<0.05). Nicotine dependence at delivery decreased from baseline levels in both groups (mean score difference, 11.7 (P=0.02) for methadone, and 16.1 (P=0.02) for slow-release morphine). All women, except 1 who had amniotic rupture, were delivered of their infant during the last trimester (mean gestation, 38 weeks). All neonates were healthy. In pregnant women who were dependent on opiates or who abused polysubstances, slow-release morphine of intermediate-length half-life did not reduce the neonatal abstinence syndrome more than methadone did. Women who received slow-release morphine used fewer additional opiates and benzodiazepines than women who received methadone.

Slow release morphine (SRM) vs methadone in pregnant women who were opiate dependent

Outcome	SRM	Methadone	RRR (95% CI)	NNT (CI)
Used additional opiates	21%	50%	58% (6-83)	4 (2-54)

RRR = relative risk reduction; NNT = number needed to treat. RRR, NNT, and CI calculated from data in article. Mean follow-up was 15 weeks (information supplied by author).

Commentary

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A recent survey in the United States showed that 5% of pregnant women used illegal drugs.[1] Despite the gravity of the problem, few empiric data exist to guide clinical management. A woman may be eager to stop drug use for fear that it will damage her unborn baby. On the other hand, the fetus is as dependent as the mother on heroin. Because the immature fetal nervous system is particularly sensitive to drug withdrawal, maintaining the fetus and mother at a stable level of opiates is preferable to in utero detoxification. Opioid maintenance treatment during pregnancy, however, only postpones the withdrawal reaction. After delivery, the neonate is still at risk of the abstinence syndrome.

We need a method that detoxifies pregnant women without causing substantial distress to the fetuses. Alternatively, we may search for an opiate that causes fewer or milder episodes of neonatal abstinence syndrome than methadone, which is currently the most commonly prescribed opiate substitute for pregnant women.

Fischer and colleagues have taken the second approach but found that slow-release morphine of intermediate-length half-life (16 hours) was not better than methadone in reducing the duration and severity of neonatal abstinence syndrome. These results are, perhaps, not surprising, given that the morphine preparation chosen has a shorter half-life than methadone (about 24 hours). Nevertheless, this study shows that slow-release morphine is superior to methadone in reducing harm. The next logical step would be to test whether slow-release morphine preparations of a long half-life are better than methadone for reducing neonatal abstinence syndrome while maintaining superiority in harm reduction.

1 Westat Inc. *National pregnancy and health survey: drug use among women delivering livebirths, 1992.* Rockville (MD): National Institute of Drug Abuse; 1996.